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<110> Jensen, Michael

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<223> Human Wild-type Inosine Monophosphate Dehydrogenase
II (IMPDH II)

<300>

<301> Collart, F.R. and Huberman, E.

<302> Cloning and sequence analysis of the human and

<303> J. Biol. Chem. (1988)

<304> 263

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 <301> Farazi et al.
 <303> J. Biol. Chem. (1997)
 <304> 271

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 Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys Gly Lys
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 Lys Tyr Arg Leu Asp Leu Leu Ala Gln Ala Gly Val Asp Val Val Val
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 Leu Asp Ser Ser Arg Gly Asn Ser Ile Phe Gln Ile Asn Met Ile Lys
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 Leu Arg Val Gly Met Gly Ser Gly Ser Ile Cys Ile Thr Gln Glu Val

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Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met Gly Ser
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Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala Val Gln
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<301> Farazi et al.
<303> J. Biol. Chem. (1997)
<304> 272
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Ala Ser Asp Ser Gly Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu	
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Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys	
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Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val	
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His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala	

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	Glu Asp Ala His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys			
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	Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala			
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	Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile			
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	tcg ggc ggc ctg gac aag cat gct gag atc cct gat ccg ctg ttc gcg			528
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	gcc act gcc ccg ctc aca gct atc ttg agt gct gtc gtt ggc gcg gca			1008
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Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly	
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 <301> Natsumeda et al.
 <302> Two Distinct cDNAs for Human IMP Dehydrogenase
 <303> J. Biol. Chem. (1990)
 <304> 265
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 <302> Cloning and Sequencing of a Human cDNA coding for
 <303> Gene (1992)
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Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly Ile Ala Ala
85      90      95
Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr Lys Met Gly
100      105      110
Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro Gln Glu Gly
115      120      125
Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln Ala Val Ile
130      135      140
Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val Glu His Arg
145      150      155      160
Leu Arg Ala Arg Gln Lys Gln Ala Lys Leu Thr Glu Asp Gly Leu
165      170      175
Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val Asp Ala Ala
180      185      190
Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu Ala Asp Tyr
195      200      205
Leu Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu Arg Ser Leu
210      215      220
Gln Gly Lys Ala Glu Leu Arg Arg Leu Leu Thr Lys Val Leu Gln Glu
225      230      235      240
Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu Val Lys Ile
245      250      255
Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala Ser Val Val
260      265      270
Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr Thr Val Ser
275      280      285
Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr Gly Gly Leu
290      295      300
Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg Glu Met
305      310      315      320
Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val Gly Gly Val
325      330      335
Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly Ala Ser Leu
340      345      350
Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro Val Val Gly
355      360      365
Lys Val Lys Arg Glu Leu Glu Ala Leu Leu Lys Glu Gln Gly Phe Gly
370      375      380
Gly Val Thr Asp Ala Ile Gly Ala Asp His Arg Arg
385      390      395

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<210> 21
 <211> 1101
 <212> DNA
 <213> Homo sapien

<220>
 <221> CDS
 <222> (1)...(1101)
 <223> DHODH Truncated 39 kDa Construct

<300>

<301> Copeland, R.A., et al.
 <302> Recombinant Human Dihydroorotate Dehydrogenase
 <303> Arch. Biochem. Biophys. (1995)
 <304> 323
 <306> 79-86

<400> 21

atg gcc acg gga gat gag cgt ttc tat gct gaa cac ctg atg ccg act	48
Met Ala Thr Gly Asp Glu Arg Phe Tyr Ala Glu His Leu Met Pro Thr	
1 5 10 15	
ctg cag ggg ctg ctg gac ccg gag tca gcc cac aga ctg gct gtt cgc	96
Leu Gln Gly Leu Leu Asp Pro Glu Ser Ala His Arg Leu Ala Val Arg	
20 25 30	
ttc acc tcc ctg ggg ctc ctt cca cgg gcc aga ttt caa gac tct gac	144
Phe Thr Ser Leu Gly Leu Leu Pro Arg Ala Arg Phe Gln Asp Ser Asp	
35 40 45	
atg ctg gaa gtg aga gtt ctg ggc cat aaa ttc cga aat cca gta gga	192
Met Leu Glu Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly	
50 55 60	
att gct gca gga ttt gac aag cat ggg gaa gcc gtg gac gga ctt tat	240
Ile Ala Ala Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr	
65 70 75 80	
aag atg ggc ttt ggt ttt gtt gag ata gga agt gtg act cca aaa cct	288
Lys Met Gly Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro	
85 90 95	
cag gaa gga aac cct aga ccc aga gtc ttc cgc ctc cct gag gac caa	336
Gln Glu Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln	
100 105 110	
gct gtc att aac agg tat gga ttt aac agt cac ggg ctt tca gtg gtg	384
Ala Val Ile Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val	
115 120 125	
gaa cac agg tta cgg gcc aga cag cag aag cag gcc aag ctc aca gaa	432
Glu His Arg Leu Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu	
130 135 140	
gat gga ctg cct ctg ggg gtc aac ttg ggg aag aac aag acc tca gtg	480
Asp Gly Leu Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val	
145 150 155 160	
gac gcc gcg gag gac tac gca gaa ggg gtg cgc gta ctg ggc ccc ctg	528
Asp Ala Ala Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu	
165 170 175	
gcc gac tac ctg gtg gtg aat gtg tcc agc ccc aac act gcc ggg ctg	576
Ala Asp Tyr Leu Val Val Asn Val Ser Pro Asn Thr Ala Gly Leu	
180 185 190	
cgg agc ctt cag gga aag gcc gag ctg cgc cgc ctg ctg acc aag gtg	624
Arg Ser Leu Gln Gly Lys Ala Glu Leu Arg Arg Leu Thr Lys Val	
195 200 205	
ctg cag gag agg gat ggc ttg cgg aga gtg cac agg ccg gca gtc ctg	672
Leu Gln Glu Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu	
210 215 220	

gtg	aag	atc	gct	cct	gac	ctc	acc	agc	cag	gat	aag	gag	gac	att	gcc	720
Val	Lys	Ile	Ala	Pro	Asp	Leu	Thr	Ser	Gln	Asp	Lys	Glu	Asp	Ile	Ala	
225					230					235					240	
agt	gtg	gtc	aaa	gag	ttg	ggc	atc	gat	ggg	ctg	att	gtt	acg	aac	acc	768
Ser	Val	Val	Lys	Glu	Leu	Gly	Ile	Asp	Gly	Leu	Ile	Val	Thr	Asn	Thr	
				245					250					255		
acc	gtg	agt	cgc	cct	gcg	ggc	ctc	cag	ggt	gcc	ctg	cgc	tct	gaa	aca	816
Thr	Val	Ser	Arg	Pro	Ala	Gly	Leu	Gln	Gly	Ala	Leu	Arg	Ser	Glu	Thr	
			260					265					270			
gga	ggg	ctg	agt	ggg	aag	ccc	ctc	cgg	gat	tta	tca	act	caa	acc	att	864
Gly	Gly	Leu	Ser	Gly	Lys	Pro	Leu	Arg	Asp	Leu	Ser	Thr	Gln	Thr	Ile	
		275					280					285				
cgg	gag	atg	tat	gca	ctc	acc	caa	ggc	cga	gtt	ccc	ata	att	ggg	gtt	912
Arg	Glu	Met	Tyr	Ala	Leu	Thr	Gln	Gly	Arg	Val	Pro	Ile	Ile	Gly	Val	
	290					295					300					
ggt	ggt	gtg	agc	agc	ggg	cag	gac	gcg	ctg	gag	aag	atc	cgg	gca	ggg	960
Gly	Gly	Val	Ser	Ser	Gly	Gln	Asp	Ala	Leu	Glu	Lys	Ile	Arg	Ala	Gly	
305					310					315					320	
gcc	tcc	ctg	gtg	cag	ctg	tac	acg	gcc	ctc	acc	ttc	tgg	ggg	cca	ccc	1008
Ala	Ser	Leu	Val	Gln	Leu	Tyr	Thr	Ala	Leu	Thr	Phe	Trp	Gly	Pro	Pro	
				325					330					335		
gtt	gtg	ggc	aaa	gtc	aag	cgg	gaa	ctg	gag	gcc	ctt	ctg	aaa	gag	cag	1056
Val	Val	Gly	Lys	Val	Lys	Arg	Glu	Leu	Glu	Ala	Leu	Leu	Lys	Glu	Gln	
			340					345					350			
ggc	ttt	ggc	gga	gtc	aca	gat	gcc	att	gga	gca	gat	cat	cgg	agg		1101
Gly	Phe	Gly	Gly	Val	Thr	Asp	Ala	Ile	Gly	Ala	Asp	His	Arg	Arg		
		355					360					365				

<210> 22
 <211> 367
 <212> PRT
 <213> Homo sapien

<400> 22
 Met Ala Thr Gly Asp Glu Arg Phe Tyr Ala Glu His Leu Met Pro Thr
 1 5 10 15
 Leu Gln Gly Leu Leu Asp Pro Glu Ser Ala His Arg Leu Ala Val Arg
 20 25 30
 Phe Thr Ser Leu Gly Leu Leu Pro Arg Ala Arg Phe Gln Asp Ser Asp
 35 40 45
 Met Leu Glu Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly
 50 55 60
 Ile Ala Ala Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr
 65 70 75 80
 Lys Met Gly Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro
 85 90 95
 Gln Glu Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln
 100 105 110
 Ala Val Ile Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val
 115 120 125
 Glu His Arg Leu Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu
 130 135 140

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Asp Gly Leu Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val
145          150          155          160
Asp Ala Ala Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu
          165          170          175
Ala Asp Tyr Leu Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu
          180          185          190
Arg Ser Leu Gln Gly Lys Ala Glu Arg Arg Leu Leu Thr Lys Val
          195          200          205
Leu Gln Glu Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu
          210          215          220
Val Lys Ile Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala
225          230          235          240
Ser Val Val Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr
          245          250          255
Thr Val Ser Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr
          260          265          270
Gly Gly Leu Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile
          275          280          285
Arg Glu Met Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val
290          295          300
Gly Gly Val Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly
305          310          315          320
Ala Ser Leu Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro
          325          330          335
Val Val Gly Lys Val Lys Arg Glu Leu Glu Ala Leu Leu Lys Glu Gln
          340          345          350
Gly Phe Gly Gly Val Thr Asp Ala Ile Gly Ala Asp His Arg Arg
          355          360          365

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<210> 23
<211> 1101
<212> DNA
<213> Homo sapien

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<220>
<221> mutation
<222> 79
<223> C to G mutation

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<221> mutation
<222> 80
<223> A to C mutation

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<221> CDS
<222> (4)...(1101)
<223> His26Ala DHODH mutant

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<300>
<301> Davis et al.
<302> Histidine to Alanine mutants of Human Dihydroorota
<303> Biochem. Pharmacol. (1997)
<304> 54
<306> 459-465

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<400> 23
atg gcc acg gga gat gag cgt ttc tat gct gaa cac ctg atg ccg act      48
  Ala Thr Gly Asp Glu Arg Phe Tyr Ala Glu His Leu Met Pro Thr
    1              5              10              15

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ctg cag ggg ctg ctg gac ccg gag tca gcc gcc aga ctg gct gtt cgc      96
Leu Gln Gly Leu Leu Asp Pro Glu Ser Ala Ala Arg Leu Ala Val Arg
          20              25              30

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ttc acc tcc ctg ggg ctc ctt cca cgg gcc aga ttt caa gac tct gac	144
Phe Thr Ser Leu Gly Leu Leu Pro Arg Ala Arg Phe Gln Asp Ser Asp	
35 40 45	
atg ctg gaa gtg aga gtt ctg ggc cat aaa ttc cga aat cca gta gga	192
Met Leu Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly	
50 55 60	
att gct gca gga ttt gac aag cat ggg gaa gcc gtg gac gga ctt tat	240
Ile Ala Ala Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr	
65 70 75	
aag atg ggc ttt ggt ttt gtt gag ata gga agt gtg act cca aaa cct	288
Lys Met Gly Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro	
80 85 90 95	
cag gaa gga aac cct aga ccc aga gtc ttc cgc ctc cct gag gac caa	336
Gln Glu Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln	
100 105 110	
gct gtc att aac agg tat gga ttt aac agt cac ggg ctt tca gtg gtg	384
Ala Val Ile Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val	
115 120 125	
gaa cac agg tta cgg gcc aga cag cag aag cag gcc aag ctc aca gaa	432
Glu His Arg Leu Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu	
130 135 140	
gat gga ctg cct ctg ggg gtc aac ttg ggg aag aac aag acc tca gtg	480
Asp Gly Leu Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val	
145 150 155	
gac gcc gcg gag gac tac gca gaa ggg gtg cgc gta ctg ggc ccc ctg	528
Asp Ala Ala Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu	
160 165 170 175	
gcc gac tac ctg gtg gtg aat gtg tcc agc ccc aac act gcc ggg ctg	576
Ala Asp Tyr Leu Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu	
180 185 190	
cgg agc ctt cag gga aag gcc gag ctg cgc cgc ctg ctg acc aag gtg	624
Arg Ser Leu Gln Gly Lys Ala Glu Leu Arg Arg Leu Leu Thr Lys Val	
195 200 205	
ctg cag gag agg gat ggc ttg cgg aga gtg cac agg ccg gca gtc ctg	672
Leu Gln Glu Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu	
210 215 220	
gtg aag atc gct cct gac ctc acc agc cag gat aag gag gac att gcc	720
Val Lys Ile Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala	
225 230 235	
agt gtg gtc aaa gag ttg ggc atc gat ggg ctg att gtt acg aac acc	768
Ser Val Val Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr	
240 245 250 255	
acc gtg agt cgc cct gcg ggc ctc cag ggt gcc ctg cgc tct gaa aca	816
Thr Val Ser Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr	
260 265 270	
gga ggg ctg agt ggg aag ccc ctc cgg gat tta tca act caa acc att	864

Gly	Gly	Leu	Ser	Gly	Lys	Pro	Leu	Arg	Asp	Leu	Ser	Thr	Gln	Thr	Ile		
			275					280					285				
cgg	gag	atg	tat	gca	ctc	acc	caa	ggc	cga	gtt	ccc	ata	att	ggg	gtt	912	
Arg	Glu	Met	Tyr	Ala	Leu	Thr	Gln	Gly	Arg	Val	Pro	Ile	Ile	Gly	Val		
		290					295					300					
ggt	ggt	gtg	agc	agc	ggg	cag	gac	gcg	ctg	gag	aag	atc	cgg	gca	ggg	960	
Gly	Gly	Val	Ser	Ser	Gly	Gln	Asp	Ala	Leu	Glu	Lys	Ile	Arg	Ala	Gly		
		305				310					315						
gcc	tcc	ctg	gtg	cag	ctg	tac	acg	gcc	ctc	acc	ttc	tgg	ggg	cca	ccc	1008	
Ala	Ser	Leu	Val	Gln	Leu	Tyr	Thr	Ala	Leu	Thr	Phe	Trp	Gly	Pro	Pro		
		320			325					330					335		
gtt	gtg	ggc	aaa	gtc	aag	cgg	gaa	ctg	gag	gcc	ctt	ctg	aaa	gag	cag	1056	
Val	Val	Gly	Lys	Val	Lys	Arg	Glu	Leu	Glu	Ala	Leu	Lys	Lys	Glu	Gln		
				340					345					350			
ggc	ttt	ggc	gga	gtc	aca	gat	gcc	att	gga	gca	gat	cat	cgg	agg		1101	
Gly	Phe	Gly	Gly	Val	Thr	Asp	Ala	Ile	Gly	Ala	Asp	His	Arg	Arg			
			355					360					365				

<210> 24
 <211> 366
 <212> PRT
 <213> Homo sapien

<400> 24

Ala	Thr	Gly	Asp	Glu	Arg	Phe	Tyr	Ala	Glu	His	Leu	Met	Pro	Thr	Leu		
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Gln	Gly	Leu	Leu	Asp	Pro	Glu	Ser	Ala	Ala	Arg	Leu	Ala	Val	Arg	Phe		
		20						25					30				
Thr	Ser	Leu	Gly	Leu	Leu	Pro	Arg	Ala	Arg	Phe	Gln	Asp	Ser	Asp	Met		
		35				40						45					
Leu	Glu	Val	Arg	Val	Leu	Gly	His	Lys	Phe	Arg	Asn	Pro	Val	Gly	Ile		
		50				55					60						
Ala	Ala	Gly	Phe	Asp	Lys	His	Gly	Glu	Ala	Val	Asp	Gly	Leu	Tyr	Lys		
				70						75					80		
Met	Gly	Phe	Gly	Phe	Val	Glu	Ile	Gly	Ser	Val	Thr	Pro	Lys	Pro	Gln		
				85					90					95			
Glu	Gly	Asn	Pro	Arg	Pro	Arg	Val	Phe	Arg	Leu	Pro	Glu	Asp	Gln	Ala		
			100					105					110				
Val	Ile	Asn	Arg	Tyr	Gly	Phe	Asn	Ser	His	Gly	Leu	Ser	Val	Val	Glu		
		115					120					125					
His	Arg	Leu	Arg	Ala	Arg	Gln	Lys	Gln	Ala	Lys	Leu	Thr	Glu	Asp			
		130				135				140							
Gly	Leu	Pro	Leu	Gly	Val	Asn	Leu	Gly	Lys	Asn	Lys	Thr	Ser	Val	Asp		
				150					155						160		
Ala	Ala	Glu	Asp	Tyr	Ala	Glu	Gly	Val	Arg	Val	Leu	Gly	Pro	Leu	Ala		
				165					170					175			
Asp	Tyr	Leu	Val	Asn	Val	Ser	Ser	Pro	Asn	Thr	Ala	Gly	Leu	Arg			
			180				185					190					
Ser	Leu	Gln	Gly	Lys	Ala	Glu	Leu	Arg	Arg	Leu	Leu	Thr	Lys	Val	Leu		
		195					200					205					
Gln	Glu	Arg	Asp	Gly	Leu	Arg	Val	His	Arg	Pro	Ala	Val	Leu	Val			
		210				215				220							
Lys	Ile	Ala	Pro	Asp	Leu	Thr	Ser	Gln	Asp	Lys	Glu	Asp	Ile	Ala	Ser		
		225			230					235					240		
Val	Val	Lys	Glu	Leu	Gly	Ile	Asp	Gly	Leu	Ile	Val	Thr	Asn	Thr	Thr		
				245					250					255			

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Val Ser Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr Gly
      260      265      270
Gly Leu Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg
      275      280      285
Glu Met Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val Gly
      290      295      300
Gly Val Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly Ala
      305      310      315      320
Ser Leu Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro Val
      325      330      335
Val Gly Lys Val Lys Arg Glu Leu Glu Ala Leu Leu Lys Glu Gln Gly
      340      345      350
Phe Gly Gly Val Thr Asp Ala Ile Gly Ala Asp His Arg Arg
      355      360      365

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<210> 25
<211> 1560
<212> DNA
<213> Aspergillus nidulans

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<220>
<221> CDS
<222> (1)...(1560)
<223> Aspergillus nidulans Val200Glu mutant DHODH cDNA

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<221> mutation
<222> 599
<223> T to A mutataation

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<400> 25
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Met Ala Thr Asn Ser Phe Arg Lys Leu Thr Phe Ser Gly Ala Ser Arg
  1          5          10          15

ctg ggt ggt tgt cgc cgt ctc cca cta acc tgc aga caa ctt cga ttc      96
Leu Gly Gly Cys Arg Arg Leu Pro Leu Thr Cys Arg Gln Leu Arg Phe
          20          25          30

gcc tcc gac agc gga gcc gca gcg gca act aca aaa gca acg gcc gaa      144
Ala Ser Asp Ser Gly Ala Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu
          35          40          45

tca gca gcc gag tca gct agt ata aac gtc aaa gag gca ccc aaa aag      192
Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys
          50          55          60

gcc gga cgg ggc ctg cgg cgc acg gtc ctg gga acg tcg ttg gcg ctg      240
Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Gly Thr Ser Leu Ala Leu
          65          70          75          80

acg ctg ctg gtt gga tat gtc tac ggg acg gac acc cgg gcg agt gtg      288
Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val
          85          90          95

cat cgg tac ggt gtt gtg ccg ctg att aga gca ttg tat cct gat gcg      336
His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala
          100          105          110

gaa gat gcg cat cat att ggt gtc gat act tta aag atg ctg tat aag      384
Glu Asp Ala His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys
          115          120          125

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tat ggt ctg cat cca agg gaa cgg ggg gat ccg gat gga gat ggg gcg Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala 130 135 140	432
ctg gcg aca gag gtc ttt ggg tat aca ctg tca aac cca att ggc ata Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile 145 150 155 160	480
tcg ggc ggc ctg gac aag cat gct gag atc cct gat ccg ctg ttc gcg Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala 165 170 175	528
atc ggt cct gcc att gtc gaa gtc ggg ggt acg aca ccc tta cca cag Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln 180 185 190	576
gat ggt aac ccg cgt cct cgc gaa ttc cga ctt cca tca cag aga gcg Asp Gly Asn Pro Arg Pro Arg Glu Phe Arg Leu Pro Ser Gln Arg Ala 195 200 205	624
atg ata aac cgg tac ggc ctc aac tcc aaa ggc gca gat cac atg gca Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala 210 215 220	672
gct atc ttg gag caa cga gta cgc gat ttt gcc tac gca aac gga ttt Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe 225 230 235 240	720
ggg gca tac gat gcg gct aag cag cgt gta ttg gac ggc gaa gct ggt Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly 245 250 255	768
gtg cca cca ggt agt ctt cag cct ggt aag ctt tta gct gtc caa gtg Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val 260 265 270	816
gca aag aac aag gcc act cct gac ggc gac att gaa gcc atc aag cgc Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg 275 280 285	864
gac tat gtg tat tgc gtg gac cgt gtg gcc aaa tac gct gat att ctt Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu 290 295 300	912
gtt gtg aat gta tcg agc ccc aac aca ccc ggt ctc cgt gac ctt caa Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln 305 310 315 320	960
gcc act gcc ccg ctc aca gct atc ttg agt gct gtc gtt ggc gcg gca Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala 325 330 335	1008
aag agc gtg aac cgc aag acc aaa cca tat gtt atg gtc aag gtc agt Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser 340 345 350	1056
ccg gat gaa gac tca gat gaa caa gtc tct ggt atc tgc gac gcc gtc Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val 355 360 365	1104
cga gca tcc ggt gtc gac gga gtg att gtc gga aac aca aca aac cgt Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg	1152

370	375	380	
cgc ccc gac cct ata ccc caa ggt tac act ctt ccg gcc aag gag cag			1200
Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln			
385	390	395	400
gca acg ttg aaa gaa acc ggc ggg tat tca ggt cca cag ctg ttc gat			1248
Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp			
	405	410	415
cgc aca gtg gcc ctt gtg gct cgg tac cgc tcc atg ctg gat gcg gag			1296
Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu			
	420	425	430
tcg gaa acg gcc gga tcc gcc aag gat tca gca gcg acc ata gcg caa			1344
Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln			
	435	440	445
aca gag cca ggc tcg gaa aac gtt cct cct gtg gaa gcg cca agc gga			1392
Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly			
	450	455	460
ctg ccg cgc aaa gtt atc ttc gct tcg ggt ggt atc acc aac ggg aag			1440
Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys			
	465	470	475
cag gct cac gct gtt tta gac aca ggg gca tct gtt gcc atg atg tac			1488
Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr			
	485	490	495
acc ggt gtg gtc tat ggt ggc gtc ggc act gtc act cga gtg aag caa			1536
Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln			
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Glu Leu Arg Thr Ala Lys Lys Glu			
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<210> 26

<211> 520

<212> PRT

<213> Aspergillus nidulans

<400> 26

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			20					25					30		
Ala	Ser	Asp	Ser	Gly	Ala	Ala	Ala	Ala	Thr	Thr	Lys	Ala	Thr	Ala	Glu
		35				40					45				
Ser	Ala	Ala	Glu	Ser	Ala	Ser	Ile	Asn	Val	Lys	Glu	Ala	Pro	Lys	Lys
	50					55				60					
Ala	Gly	Arg	Gly	Leu	Arg	Arg	Thr	Val	Leu	Gly	Thr	Ser	Leu	Ala	Leu
65				70					75					80	
Thr	Leu	Leu	Val	Gly	Tyr	Val	Tyr	Gly	Thr	Asp	Thr	Arg	Ala	Ser	Val
			85					90					95		
His	Arg	Tyr	Gly	Val	Val	Pro	Leu	Ile	Arg	Ala	Leu	Tyr	Pro	Asp	Ala
		100						105					110		
Glu	Asp	Ala	His	His	Ile	Gly	Val	Asp	Thr	Leu	Lys	Met	Leu	Tyr	Lys
		115				120						125			
Tyr	Gly	Leu	His	Pro	Arg	Glu	Arg	Gly	Asp	Pro	Asp	Gly	Asp	Gly	Ala

130	135	140
Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile		
145	150	155
Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala		
	165	170
Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln		
	180	185
Asp Gly Asn Pro Arg Pro Arg Glu Phe Arg Leu Pro Ser Gln Arg Ala		
	195	200
Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala		
	210	215
Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe		
225	230	235
Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly		
	245	250
Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val		
	260	265
Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg		
	275	280
Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu		
	290	295
Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln		
305	310	315
Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala		
	325	330
Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser		
	340	345
Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val		
	355	360
Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg		
	370	375
Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln		
385	390	395
Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp		
	405	410
Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu		
	420	425
Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln		
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Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly		
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Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys		
465	470	475
Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr		
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Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln		
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Glu Leu Arg Thr Ala Lys Lys Glu		
515	520	

<210> 27

<211> 1560

<212> DNA

<213> Aspergillus nidulans

<220>

<221> CDS

<222> (1)...(1560)

<223> Aspergillus nidulans Ala115Val mutant DHODH cDNA

<221> mutation

<222> 344

<223> C to T mutation

<400> 27

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ctg ggt ggt tgt cgc cgt ctc cca cta acc tgc aga caa ctt cga ttc	96
Leu Gly Gly Cys Arg Arg Leu Pro Leu Thr Cys Arg Gln Leu Arg Phe	
20 25 30	
gcc tcc gac agc gga gcc gca gcg gca act aca aaa gca acg gcc gaa	144
Ala Ser Asp Ser Gly Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu	
35 40 45	
tca gca gcc gag tca gct agt ata aac gtc aaa gag gca ccc aaa aag	192
Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys	
50 55 60	
gcc gga cgg ggc ctg cgg cgc acg gtc ctg gga acg tcg ttg gcg ctg	240
Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Thr Ser Leu Ala Leu	
65 70 75 80	
acg ctg ctg gtt gga tat gtc tac ggg acg gac acc cgg gcg agt gtg	288
Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val	
85 90 95	
cat cgg tac ggt gtt gtg ccg ctg att aga gca ttg tat cct gat gcg	336
His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala	
100 105 110	
gaa gat gtg cat cat att ggt gtc gat act tta aag atg ctg tat aag	384
Glu Asp Val His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys	
115 120 125	
tat ggt ctg cat cca agg gaa cgg ggg gat ccg gat gga gat ggg gcg	432
Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala	
130 135 140	
ctg gcg aca gag gtc ttt ggg tat aca ctg tca aac cca att ggc ata	480
Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile	
145 150 155 160	
tcg ggc ggc ctg gac aag cat gct gag atc cct gat ccg ctg ttc gcg	528
Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala	
165 170 175	
atc ggt cct gcc att gtc gaa gtc ggg ggt acg aca ccc tta cca cag	576
Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln	
180 185 190	
gat ggt aac ccg cgt cct cgc gta ttc cga ctt cca tca cag aga gcg	624
Asp Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Ser Gln Arg Ala	
195 200 205	
atg ata aac cgg tac ggc ctc aac tcc aaa ggc gca gat cac atg gca	672
Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala	
210 215 220	
gct atc ttg gag caa cga gta cgc gat ttt gcc tac gca aac gga ttt	720
Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe	
225 230 235 240	

ggg gca tac gat gcg gct aag cag cgt gta ttg gac ggc gaa gct ggt	768
Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly	
245 250 255	
gtg cca cca ggt agt ctt cag cct ggt aag ctt tta gct gtc caa gtg	816
Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val	
260 265 270	
gca aag aac aag gcc act cct gac ggc gac att gaa gcc atc aag cgc	864
Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg	
275 280 285	
gac tat gtg tat tgc gtg gac cgt gtg gcc aaa tac gct gat att ctt	912
Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu	
290 295 300	
gtt gtg aat gta tcg agc ccc aac aca ccc ggt ctc cgt gac ctt caa	960
Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln	
305 310 315 320	
gcc act gcc ccg ctc aca gct atc ttg agt gct gtc gtt ggc gcg gca	1008
Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala	
325 330 335	
aag agc gtg aac cgc aag acc aaa cca tat gtt atg gtc aag gtc agt	1056
Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser	
340 345 350	
ccg gat gaa gac tca gat gaa caa gtc tct ggt atc tgc gac gcc gtc	1104
Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val	
355 360 365	
cga gca tcc ggt gtc gac gga gtg att gtc gga aac aca aca aac cgt	1152
Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg	
370 375 380	
cgc ccc gac cct ata ccc caa ggt tac act ctt ccg gcc aag gag cag	1200
Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln	
385 390 400	
gca acg ttg aaa gaa acc ggc ggg tat tca ggt cca cag ctg ttc gat	1248
Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp	
405 410 415	
cgc aca gtg gcc ctt gtg gct cgg tac cgc tcc atg ctg gat gcg gag	1296
Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu	
420 425 430	
tcg gaa acg gcc gga tcc gcc aag gat tca gca gcg acc ata gcg caa	1344
Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln	
435 440 445	
aca gag cca ggc tcg gaa aac gtt cct cct gtg gaa gcg cca agc gga	1392
Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly	
450 455 460	
ctg ccg cgc aaa gtt atc ttc gct tcg ggt ggt atc acc aac ggg aag	1440
Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys	
465 470 475 480	
cag gct cac gct gtt tta gac aca ggg gca tct gtt gcc atg atg tac	1488

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Glu Leu Arg Thr Ala Lys Lys Glu
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<211> 520
<212> PRT
<213> Aspergillus nidulans
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			20					25					30		
Ala	Ser	Asp	Ser	Gly	Ala	Ala	Ala	Ala	Thr	Thr	Lys	Ala	Thr	Ala	Glu
		35				40						45			
Ser	Ala	Ala	Glu	Ser	Ala	Ser	Ile	Asn	Val	Lys	Glu	Ala	Pro	Lys	Lys
	50					55					60				
Ala	Gly	Arg	Gly	Leu	Arg	Arg	Thr	Val	Leu	Gly	Thr	Ser	Leu	Ala	Leu
65				70						75					80
Thr	Leu	Leu	Val	Gly	Tyr	Val	Tyr	Gly	Thr	Asp	Thr	Arg	Ala	Ser	Val
			85					90						95	
His	Arg	Tyr	Gly	Val	Val	Pro	Leu	Ile	Arg	Ala	Leu	Tyr	Pro	Asp	Ala
			100					105					110		
Glu	Asp	Val	His	His	Ile	Gly	Val	Asp	Thr	Leu	Lys	Met	Leu	Tyr	Lys
		115					120					125			
Tyr	Gly	Leu	His	Pro	Arg	Glu	Arg	Gly	Asp	Pro	Asp	Gly	Asp	Gly	Ala
	130					135					140				
Leu	Ala	Thr	Glu	Val	Phe	Gly	Tyr	Thr	Leu	Ser	Asn	Pro	Ile	Gly	Ile
145					150					155					160
Ser	Gly	Gly	Leu	Asp	Lys	His	Ala	Glu	Ile	Pro	Asp	Pro	Leu	Phe	Ala
				165					170					175	
Ile	Gly	Pro	Ala	Ile	Val	Glu	Val	Gly	Gly	Thr	Thr	Pro	Leu	Pro	Gln
			180					185					190		
Asp	Gly	Asn	Pro	Arg	Pro	Arg	Val	Phe	Arg	Leu	Pro	Ser	Gln	Arg	Ala
		195					200					205			
Met	Ile	Asn	Arg	Tyr	Gly	Leu	Asn	Ser	Lys	Gly	Ala	Asp	His	Met	Ala
	210					215					220				
Ala	Ile	Leu	Glu	Gln	Arg	Val	Arg	Asp	Phe	Ala	Tyr	Ala	Asn	Gly	Phe
225				230						235					240
Gly	Ala	Tyr	Asp	Ala	Ala	Lys	Gln	Arg	Val	Leu	Asp	Gly	Glu	Ala	Gly
				245					250					255	
Val	Pro	Pro	Gly	Ser	Leu	Gln	Pro	Gly	Lys	Leu	Leu	Ala	Val	Gln	Val
			260					265					270		
Ala	Lys	Asn	Lys	Ala	Thr	Pro	Asp	Gly	Asp	Ile	Glu	Ala	Ile	Lys	Arg
		275					280					285			
Asp	Tyr	Val	Tyr	Cys	Val	Asp	Arg	Val	Ala	Lys	Tyr	Ala	Asp	Ile	Leu
	290					295					300				
Val	Val	Asn	Val	Ser	Ser	Pro	Asn	Thr	Pro	Gly	Leu	Arg	Asp	Leu	Gln
305				310						315					320
Ala	Thr	Ala	Pro	Leu	Thr	Ala	Ile	Leu	Ser	Ala	Val	Val	Gly	Ala	Ala
				325					330					335	
Lys	Ser	Val	Asn	Arg	Lys	Thr	Lys	Pro	Tyr	Val	Met	Val	Lys</		

Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val
 355 360 365
 Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg
 370 375 380
 Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln
 385 390 395 400
 Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp
 405 410 415
 Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu
 420 425 430
 Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln
 435 440 445
 Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly
 450 455 460
 Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys
 465 470 475 480
 Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr
 485 490 495
 Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln
 500 505 510
 Glu Leu Arg Thr Ala Lys Lys Glu
 515 520

<210> 29

<211> 1707

<212> DNA

<213> Mus musculus

<220>

<221> CDS

<222> (67)...(1611)

<223> wild-type IMP dehydrogenase cDNA

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 Met Ala Asp Tyr Leu Ile Ser Gly Gly Thr Ser Tyr Val Pro

1

5

10

gac gac ggg ctc aca gcg cag cag ctc ttc aac tgc ggg gac ggc ctc 156
 Asp Asp Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu
 15 20 25 30

acc tac aat gat ttt ctc att ctt cct ggg tat atc gac ttc act gca 204
 Thr Tyr Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala
 35 40 45

gat cag gtg gac ttg acg tct gct cta act aag aag att aca cta aag 252
 Asp Gln Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys
 50 55 60

acc cca ttg gtt tcc tca ccc atg gac act gtc aca gag gct gga atg 300
 Thr Pro Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met
 65 70 75

gcc atc gcg atg gcg ctt aca gga ggt att ggt ttc atc cac cac aac 348
 Ala Ile Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn
 80 85 90

tgc aca cct gaa ttc cag gcc aat gaa gtt cgg aaa gtg aag aaa tac 396
 Cys Thr Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr
 95 100 105 110

gaa	cag	gga	ttc	atc	act	gac	ccc	gtg	gtc	ctt	agc	ccc	aag	gat	cgt	444
Glu	Gln	Gly	Phe	Ile	Thr	Asp	Pro	Val	Val	Leu	Ser	Pro	Lys	Asp	Arg	
				115					120					125		
gta	cgc	gat	gtt	ttt	gag	gcc	aaa	gcc	agg	cat	ggc	ttc	tgt	ggg	atc	492
Val	Arg	Asp	Val	Phe	Glu	Ala	Lys	Ala	Arg	His	Gly	Phe	Cys	Gly	Ile	
			130					135					140			
ccc	atc	aca	gat	aca	ggc	cgg	atg	ggg	agt	cga	ttg	gtg	ggc	atc	atc	540
Pro	Ile	Thr	Asp	Thr	Gly	Arg	Met	Gly	Ser	Arg	Leu	Val	Gly	Ile	Ile	
		145					150					155				
tcc	tca	agg	gac	att	gat	ttc	ctc	aag	gag	gaa	gag	cat	gac	cgg	ttc	588
Ser	Ser	Arg	Asp	Ile	Asp	Phe	Leu	Lys	Glu	Glu	Glu	His	Asp	Arg	Phe	
	160					165					170					
ttg	gaa	gag	atc	atg	act	aag	agg	gaa	gat	ttg	gtg	gtc	gcc	cct	gcc	636
Leu	Glu	Glu	Ile	Met	Thr	Lys	Arg	Glu	Asp	Leu	Val	Val	Ala	Pro	Ala	
175					180				185						190	
ggc	gtc	act	ctg	aaa	gag	gca	aat	gag	att	ctg	cag	cga	agt	aaa	aag	684
Gly	Val	Thr	Leu	Lys	Glu	Ala	Asn	Glu	Ile	Leu	Gln	Arg	Ser	Lys	Lys	
				195					200					205		
gga	aag	ttg	ccc	att	gtg	aat	gaa	aat	gat	gag	ctg	gta	gcc	atc	att	732
Gly	Lys	Leu	Pro	Ile	Val	Asn	Glu	Asn	Asp	Glu	Leu	Val	Ala	Ile	Ile	
			210					215					220			
gcc	cgg	aca	gac	cta	aag	aag	aat	cgt	gat	tac	ccc	ctg	gcc	tcc	aaa	780
Ala	Arg	Thr	Asp	Leu	Lys	Lys	Asn	Arg	Asp	Tyr	Pro	Leu	Ala	Ser	Lys	
		225					230					235				
gat	gcc	aag	aag	caa	ctg	ctg	tgt	ggg	gca	gcc	att	ggc	act	cat	gag	828
Asp	Ala	Lys	Lys	Gln	Leu	Leu	Cys	Gly	Ala	Ala	Ile	Gly	Thr	His	Glu	
	240					245					250					
gat	gac	aag	tat	agg	ctg	gac	tta	ctg	gcc	ctt	gct	ggg	gtg	gat	gta	876
Asp	Asp	Lys	Tyr	Arg	Leu	Asp	Leu	Leu	Ala	Leu	Ala	Gly	Val	Asp	Val	
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gtg	gtt	ttg	gac	tct	tcc	cag	gga	aac	tcc	atc	ttc	caa	atc	aat	atg	924
Val	Val	Leu	Asp	Ser	Ser	Gln	Gly	Asn	Ser	Ile	Phe	Gln	Ile	Asn	Met	
				275					280					285		
atc	aaa	tac	atc	aag	gag	aag	tat	ccc	agt	cta	cag	gtc	att	gga	ggc	972
Ile	Lys	Tyr	Ile	Lys	Glu	Lys	Tyr	Pro	Ser	Leu	Gln	Val	Ile	Gly	Gly	
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aat	gta	gtc	act	gct	gcg	caa	gcc	aag	aac	ctc	ata	gat	gca	ggg	gta	1020
Asn	Val	Val	Thr	Ala	Ala	Gln	Ala	Lys	Asn	Leu	Ile	Asp	Ala	Gly	Val	
		305					310					315				
gat	gct	ttg	cga	gtc	ggc	atg	gga	agt	ggg	tcc	atc	tgc	atc	acc	cag	1068
Asp	Ala	Leu	Arg	Val	Gly	Met	Gly	Ser	Gly	Ser	Ile	Cys	Ile	Thr	Gln	
	320					325					330					
gaa	gtg	ttg	gcc	tgt	ggg	cgg	ccc	caa	gcc	aca	gca	gtg	tac	aag	gtc	1116
Glu	Val	Leu	Ala	Cys	Gly	Arg	Pro	Gln	Ala	Thr	Ala	Val	Tyr	Lys	Val	
335					340					345					350	
tct	gag	tat	gcc	cgt	cgc	ttt	ggg	gtt	cct	gtt	att	gct	gat	gga	gga	1164

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Ile Gln Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser
      370      375      380
aca gtc atg atg ggc tcc ctc ctg gct gcc acc act gag gcc cct ggc 1260
Thr Val Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly
      385      390      395
gag tac ttc ttc tca gat ggg atc cgg ctg aag aaa tac cga ggt atg 1308
Glu Tyr Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met
      400      405      410
ggg tct ctt gat gcc atg gac aaa cat ctc agc agc cag aac cga tac 1356
Gly Ser Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr
      415      420      425      430
ttc agt gaa gct gac aaa atc aaa gtg gcc caa gga gtt tca ggg gca 1404
Phe Ser Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala
      435      440      445
gtg cag gac aag ggg tct atc cac aag ttc gtt cct tac ctg att gct 1452
Val Gln Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala
      450      455      460
ggc atc cag cat tcc tgt caa gac att ggt gcc aag agt tta acc caa 1500
Gly Ile Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln
      465      470      475
gtc aga gcc atg acg tac tcg ggg gag ctt aaa ttt gag aag agg aca 1548
Val Arg Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr
      480      485      490
tcc tct gct cag gtg gaa ggt ggc gtc cac agc ctc cat tcg tac gag 1596
Ser Ser Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu
      495      500      505      510
aaa cgg ctt ttc tga aaacagatcc agtatatgcc ttgaattttt caataaaagt 1651
Lys Arg Leu Phe *

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<211> 514
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<212> PRT
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<213> Mus musculus
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<400> 30
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      20      25      30
Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala Asp Gln
      35      40      45
Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro
      50      55      60
Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile
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 <222> (67)...(1611)
 <223> mouse IMP dehydrogenase cDNA double mutant:
 Thr333Ile
 Ser351Tyr

<221> mutation
 <222> 1064
 <223> C to T mutation

<221> mutation
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 <223> C to A mutation

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 Met Ala Asp Tyr Leu Ile Ser Gly Gly Thr Ser Tyr Val Pro
 1 5 10

gac gac ggg ctc aca gcg cag cag ctc ttc aac tgc ggg gac ggc ctc 156
 Asp Asp Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu
 15 20 25 30

acc tac aat gat ttt ctc att ctt cct ggg tat atc gac ttc act gca 204
 Thr Tyr Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala
 35 40 45

gat cag gtg gac ttg acg tct gct cta act aag aag att aca cta aag 252
 Asp Gln Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys
 50 55 60

acc cca ttg gtt tcc tca ccc atg gac act gtc aca gag gct gga atg 300
 Thr Pro Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met
 65 70 75

gcc atc gcg atg gcg ctt aca gga ggt att ggt ttc atc cac cac aac 348
 Ala Ile Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn
 80 85 90

tgc aca cct gaa ttc cag gcc aat gaa gtt cgg aaa gtg aag aaa tac 396
 Cys Thr Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr
 95 100 105 110

gaa cag gga ttc atc act gac ccc gtg gtc ctt agc ccc aag gat cgt 444
 Glu Gln Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg
 115 120 125

gta cgc gat gtt ttt gag gcc aaa gcc agg cat ggc ttc tgt ggt atc 492
 Val Arg Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile
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ccc atc aca gat aca ggc cgg atg ggg agt cga ttg gtg ggc atc atc 540
 Pro Ile Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile
 145 150 155

tcc tca agg gac att gat ttc ctc aag gag gaa gag cat gac cgg ttc 588
 Ser Ser Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Arg Phe
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ttg gaa gag atc atg act aag agg gaa gat ttg gtg gtc gcc cct gcc 636
 Leu Glu Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala

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aca gtc atg atg ggc tcc ctc ctg gct gcc acc act gag gcc cct ggc Thr Val Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly 385 390 395				1260
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ggt tct ctt gat gcc atg gac aaa cat ctc agc agc cag aac cga tac Gly Ser Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr 415 420 425 430				1356

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 Gly Ile Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln
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 gtc aga gcc atg acg tac tcg ggg gag ctt aaa ttt gag aag agg aca 1548
 Val Arg Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr
 480 485 490
 tcc tct gct cag gtg gaa ggt ggc gtc cac agc ctc cat tcg tac gag 1596
 Ser Ser Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu
 495 500 505 510
 aaa cgg ctt ttc tga aaacagatcc agtatatgcc ttgaattttt caataaaagt 1651
 Lys Arg Leu Phe *

ttgggaaaaa aaaagtgaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 1707

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 <212> PRT
 <213> Mus musculus

<400> 32
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 35 40 45
 Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro
 50 55 60
 Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile
 65 70 75 80
 Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn Cys Thr
 85 90 95
 Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr Glu Gln
 100 105 110
 Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg
 115 120 125
 Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile
 130 135 140
 Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser
 145 150 155 160
 Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Arg Phe Leu Glu
 165 170 175
 Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala Gly Val
 180 185 190
 Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys Gly Lys
 195 200 205
 Leu Pro Ile Val Asn Glu Asn Asp Glu Leu Val Ala Ile Ile Ala Arg
 210 215 220
 Thr Asp Leu Lys Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys Asp Ala
 225 230 235 240

Lys Lys Gln Leu Leu Cys Gly Ala Ala Ile Gly Thr His Glu Asp Asp
 245 250 255
 Lys Tyr Arg Leu Asp Leu Leu Ala Leu Ala Gly Val Asp Val Val Val
 260 265 270
 Leu Asp Ser Ser Gln Gly Asn Ser Ile Phe Gln Ile Asn Met Ile Lys
 275 280 285
 Tyr Ile Lys Glu Lys Tyr Pro Ser Leu Gln Val Ile Gly Gly Asn Val
 290 295 300
 Val Thr Ala Ala Gln Ala Lys Asn Leu Ile Asp Ala Gly Val Asp Ala
 305 310 315 320
 Leu Arg Val Gly Met Gly Ser Gly Ser Ile Cys Ile Ile Gln Glu Val
 325 330 335
 Leu Ala Cys Gly Arg Pro Gln Ala Thr Ala Val Tyr Lys Val Tyr Glu
 340 345 350
 Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Ile Gln
 355 360 365
 Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser Thr Val
 370 375 380
 Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly Glu Tyr
 385 390 395 400
 Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met Gly Ser
 405 410 415
 Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr Phe Ser
 420 425 430
 Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala Val Gln
 435 440 445
 Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala Gly Ile
 450 455 460
 Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln Val Arg
 465 470 475 480
 Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr Ser Ser
 485 490 495
 Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu Lys Arg
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 Leu Phe

<210> 33
 <211> 5627
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Sequence of pMG
 plasmid from InvivoGen

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<211> 40
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Forward primer for amplification-based cloning of hIMPDPH type II cDNA

<400> 34
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<210> 35
 <211> 33
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Reverse primer for amplification-based cloning of hIMPDPH type II cDNA

<400> 35
 catactcttc gccgaaaaga ctagatctcg atc 33

<210> 36
 <211> 32
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Forward primer for T333I mutation of hIMPDPH type II cDNA

<400> 36
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<210> 37
 <211> 32
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Reverse primer for T333I mutation of hIMPDPH type II cDNA

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<210> 38
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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Forward primer for S351Y mutation of hIMPDPH type II cDNA

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cagcagtgtgta caaggtgtat gagtatgcac ggcgcttt

38

<210> 39

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Reverse primer for S351Y mutation of hIMPDPH type II cDNA

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39